The following vignette applies to the next **2** items. The items in the set must be answered in sequential order. Once you click **Proceed to Next Item**, you will not be able to add or change an answer.

A 24-year-old woman comes to the office for an infertility evaluation. She has had irregular menstrual cycles for the past 5 years, with menstrual periods every 2-3 months on average. Her past medical history is notable for an appendectomy 5 years ago but is otherwise not significant. The patient takes no medications. Her blood pressure is 125/86 mm Hg and pulse is 72/min. BMI is 33 kg/m^2. Physical examination shows facial acne and excessive hair growth on the upper lip and chin.

Item 1 of 2

Which of the following is the most likely pathologic finding in this patient?

- A. Atrophic endometrium
- B. Bilateral adrenal atrophy
- C. Enlarged ovaries
- D. Pituitary adenoma
- E. Polycystic kidneys

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Item 1 of 2

Which of the following is the most likely pathologic finding in this patient?

- A. Atrophic endometrium (4%)
- B. Bilateral adrenal atrophy (1%)
- ✓ C. Enlarged ovaries (77%)
- D. Pituitary adenoma (4%)
- E. Polycystic kidneys (12%)

Omitted
Correct answer
C

77%
Answered correctly

02 secs
Time Spent

01/20/2020
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Explanation

Polycystic ovary syndrome	
Clinical features	• **Androgen excess**: Hirsutism, acne, androgenic alopecia • **Ovarian dysfunction**: Menstrual irregularity, polycystic ovaries • **Insulin resistance**: Acanthosis nigricans, glucose intolerance/diabetes, metabolic syndrome • **Obesity**
Treatment	• Weight loss • Combination hormonal contraceptives • Metformin (if hyperglycemia/diabetes)

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This patient with obesity, menstrual irregularities, and hirsutism most likely has **polycystic ovary syndrome** (PCOS). The etiology of PCOS is heterogeneous and multifactorial and involves both genetic and environmental factors (eg, diet, obesity).

PCOS is characterized by a number of hormonal abnormalities that may be present to varying degrees. LH levels are typically elevated, and patients may also have increased LH activity at the ovary (increased LH receptor expression). Most patients also have insulin resistance and elevated insulin levels, often with obesity, dyslipidemia, and an increased risk of diabetes and cardiovascular disease. PCOS is also characterized by increased ovarian and/or adrenal **androgen production**, likely due to the effects of LH, insulin, and possibly additional genetic factors. In addition to systemic manifestations (eg, acne, hirsutism, male-pattern hair loss), excess androgen levels in the ovaries cause anovulation/infertility, oligomenorrhea, and enlarged ovaries with multiple cysts.

(Choice A) Estrogen levels are also elevated chronically in patients with PCOS. This may cause endometrial hyperplasia and possibly an increased risk of endometrial carcinoma.

(Choices B and D) Cushing syndrome (CS) is caused by cortisol excess, usually due to a hyperfunctioning adrenal adenoma or an ACTH-producing pituitary adenoma. CS and PCOS share several clinical features, such as obesity, hirsutism, and menstrual irregularities. However,

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(Choices B and D) Cushing syndrome (CS) is caused by cortisol excess, usually due to a hyperfunctioning adrenal adenoma or an ACTH-producing pituitary adenoma. CS and PCOS share several clinical features, such as obesity, hirsutism, and menstrual irregularities. However, patients with CS typically also have moon facies, enlarged supraclavicular and dorsocervical fat pads, skin atrophy, and proximal muscle weakness. CS due to an adrenal adenoma may cause contralateral adrenal atrophy but not bilateral atrophy.

(Choice E) Polycystic kidney disease is an inherited condition with juvenile and adult forms. Patients typically have hypertension, flank pain, recurrent urinary tract infections, hematuria, and renal insufficiency.

Educational objective:
Polycystic ovary syndrome is characterized by elevated LH levels, excess androgen production, and insulin resistance. Clinical features include obesity, menstrual irregularities, hirsutism, enlarged ovaries, and an increased risk of diabetes mellitus and endometrial hyperplasia.

References

- Polycystic ovarian syndrome.

Pathophysiology	Female Reproductive System & Breast	Polycystic ovary disease
Subject	System	Topic

Item 2 of 2

The patient wishes to discuss treatment options. Which of the following treatment mechanisms best addresses her infertility problem?

A. 11-beta-hydroxylase antagonism

B. Androgen receptor antagonism

C. Dopamine receptor agonism

D. Estrogen receptor modulation

E. Progesterone supplementation

Submit

Item 2 of 2

The patient wishes to discuss treatment options. Which of the following treatment mechanisms best addresses her infertility problem?

A. 11-beta-hydroxylase antagonism (1%)

B. Androgen receptor antagonism (31%)

C. Dopamine receptor agonism (1%)

✓ D. Estrogen receptor modulation (43%)

E. Progesterone supplementation (22%)

Omitted
Correct answer
D

43%
Answered correctly

02 secs
Time Spent

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Explanation

Patients who are obese and have polycystic ovary syndrome (PCOS) should be advised on **weight loss**, which can often reverse insulin resistance and restore normal ovulatory function. Those who do not wish to become pregnant may also be started on dual estrogen-progestin **oral contraceptive pills** to minimize endometrial proliferation, reduce androgenic symptoms (eg, hirsutism, acne), and prevent unwanted pregnancy.

For those who do wish to become pregnant, if weight loss does not restore ovulation, medications aimed at inducing ovulation (eg, clomiphene, letrozole) are used. **Clomiphene** is a selective estrogen receptor modulator that prevents negative feedback inhibition on the hypothalamus and pituitary by circulating estrogen, resulting in increased gonadotropin production (FSH and LH) and ovulation.

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(Choice A) Metyrapone, an 11-beta-hydroxylase inhibitor, blocks synthesis of cortisol. The resulting increase in pituitary ACTH release leads to increased adrenal androgen production and would worsen androgenic symptoms.

(Choice B) Spironolactone is an androgen receptor antagonist used in the treatment of acne and hirsutism for PCOS patients who do not respond adequately to oral contraceptive pills. It is not used in those who wish to become pregnant due to the risk of fetal abnormalities.

(Choice C) Dopamine agonists (eg, bromocriptine, cabergoline) decrease pituitary release of prolactin and are useful in patients with infertility due to hyperprolactinemia. They are not useful in PCOS.

(Choice E) Progestin-only medications directly inhibit the endometrium and can be used to minimize endometrial hyperplasia in patients with PCOS. However, these medications would not enhance fertility and, unlike dual estrogen-progestin medications, would not improve hirsutism and acne.

Educational objective:
Patients with polycystic ovary syndrome who desire fertility can be treated with clomiphene. Clomiphene is an estrogen receptor modulator that decreases negative feedback inhibition on the hypothalamus by circulating estrogen, thereby increasing gonadotropin production.

References

- The treatment of infertility in polycystic ovary syndrome: a brief update.

Pathophysiology	Female Reproductive System & Breast	Polycystic ovary disease
Subject	System	Topic

A 33-year-old woman comes to a fertility clinic for evaluation. She has been attempting to conceive for 1 year with her current partner of 5 years without success. Her monogamous partner has been found to have adequate sperm motility, volume, and count. The patient used oral contraceptives for 15 years but stopped a year ago. Seven years ago, she received ceftriaxone for fever, abdominal pain, and vaginal discharge. Which of the following is the most likely major contributing factor to her inability to conceive?

A. Advanced maternal age

B. Congenital absence of the vas deferens

C. Inadequate time for attempted conception

D. Insufficient antibiotic therapy

E. Long-term oral contraceptive use

Submit

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- A. Advanced maternal age (2%)
- B. Congenital absence of the vas deferens (0%)
- C. Inadequate time for attempted conception (4%)
- ✓ D. Insufficient antibiotic therapy (78%)
- E. Long-term oral contraceptive use (13%)

Omitted
Correct answer
D

78%
Answered correctly

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Explanation

Pelvic inflammatory disease	
Symptoms	• Lower abdominal pain • Abnormal bleeding
Physical examination	• Cervical motion tenderness • Fever >38.3 C (>100.9 F)

Pelvic inflammatory disease	
Symptoms	• Lower abdominal pain • Abnormal bleeding
Physical examination	• Cervical motion tenderness • Fever >38.3 C (>100.9 F) • Mucopurulent cervical discharge
Treatment	• Third-generation cephalosporin ***plus*** • Azithromycin ***or*** doxycycline
Complications	• Tubo-ovarian abscess • Infertility • Ectopic pregnancy • Perihepatitis

Pelvic inflammatory disease (PID) is most frequently caused by *Neisseria gonorrhoeae* and *Chlamydia trachomatis*. Infection by both organisms can be asymptomatic or cause PID or cervicitis. PID involves inflammation of the endometrium, fallopian tubes, and/or peritoneal cavity (eg, Fitz-Hugh-Curtis syndrome). PID is the most common cause of **tubal-factor infertility**. Ectopic pregnancy is another potential significant consequence of untreated infection and tubal scarring.

This patient's history of fever, abdominal pain, and discharge is highly characteristic of PID. Treatment must always include coverage of both *C trachomatis* and *N gonorrhoeae* as **coinfection** is common. A third-generation **cephalosporin** will treat the gonococcal infection, and further treatment with **azithromycin or doxycycline** is required to treat the chlamydia, which is not sensitive to beta-lactams. This patient was treated with only a cephalosporin (eg, ceftriaxone), and she likely had an ongoing asymptomatic or subclinical infection. Even if adequate treatment was provided, long-term sequelae may not have been prevented due to scarring and adhesion formation from the healing of inflamed tissues. As a result, this patient likely had **fallopian tube** scarring/occlusion, loss of ciliary action, and subsequent infertility.

- Perihepatitis

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(Choice A) Advanced maternal age is an important factor contributing to decreased fertility as women approach menopause (average age 51). The decrease in fecundity after age 35 is primarily due to the diminishing quantity and quality of oocytes.

(Choice B) Congenital absence of the vas deferens is characterized by low sperm volume and acidic pH of an ejaculate sample. This patient's partner has adequate sperm volume and is therefore unlikely to have congenital absence of the vas deferens.

(Choice C) This patient has been attempting to conceive for 1 year. Most couples having unprotected intercourse will successfully conceive within 1 year.

(Choice E) Oral contraceptive use is not associated with ovarian failure. The menstrual cycle and fertility should return to normal shortly after the contraceptive is discontinued. However, premature ovarian failure (eg, primary ovarian insufficiency) can occur in women who smoke or those receiving radiation or chemotherapy.

Educational objective:
Pelvic inflammatory disease (PID) is most frequently caused by *Neisseria gonorrhoeae* and *Chlamydia trachomatis*. Severe or inadequately treated PID can result in fallopian tube scarring, which in turn can lead to infertility. Treatment must always include coverage of both organisms with a third-generation cephalosporin (eg, ceftriaxone) as well as azithromycin or doxycycline.

References

- Pelvic pain

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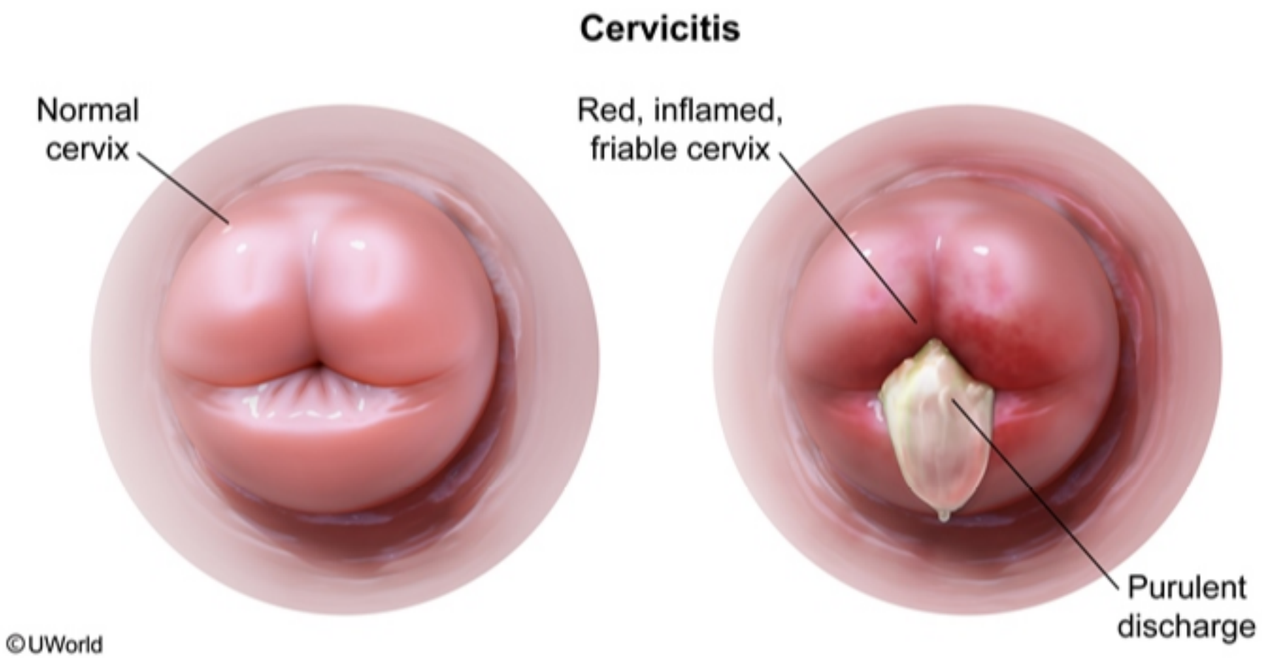

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References

- Pelvic pathologies

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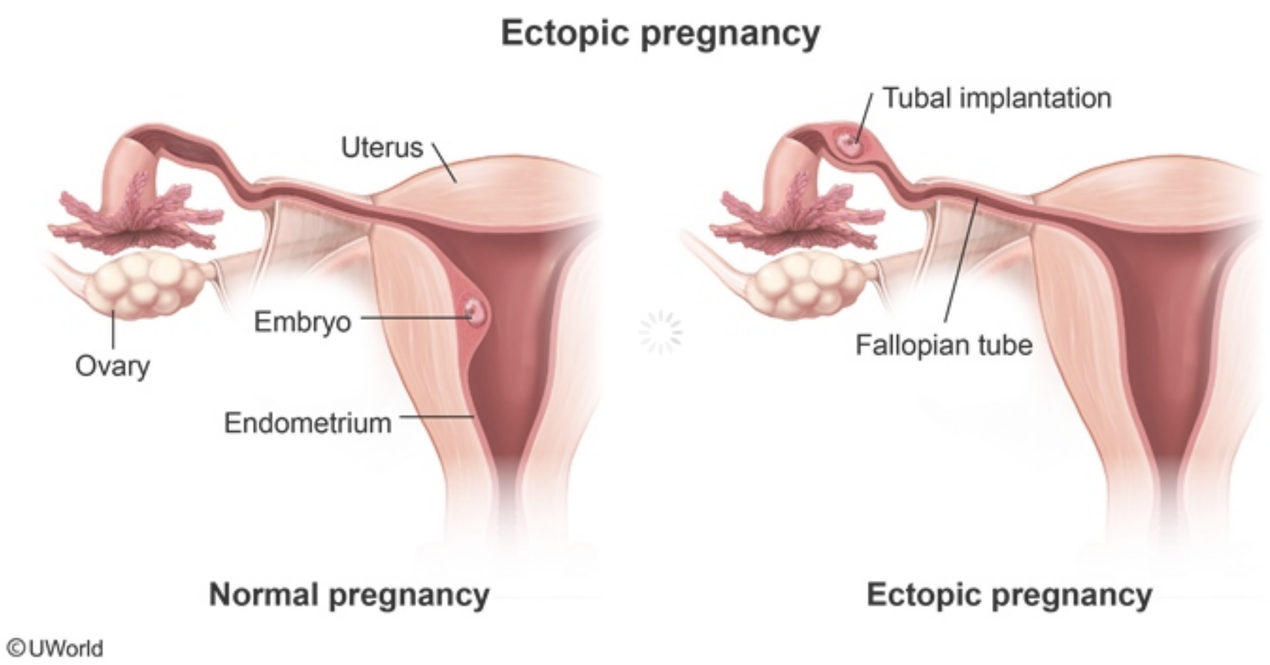

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References

A 55-year-old woman comes to the office due to vaginal bleeding. The patient underwent menopause at age 49 but has had intermittent, light vaginal bleeding for the last 6 months. She has no pelvic pain and otherwise feels well. The patient has type 2 diabetes mellitus, which is managed with diet and exercise. Vital signs are normal. BMI is 38 kg/m^2. Speculum examination shows dark red blood at the cervical os. On bimanual examination, the uterus is small and nontender and there are no palpable adnexal masses. Which of the following is the most likely underlying cause of this patient's symptoms?

A. Autonomous pituitary secretion of prolactin

B. Ectopic implantation of endometrial glands and stroma

C. Elevated sex-hormone binding globulin levels

D. Increased peripheral aromatization of androgens

E. Suppression of hypothalamic GnRH secretion

Submit

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- A. Autonomous pituitary secretion of prolactin (0%)
- B. Ectopic implantation of endometrial glands and stroma (19%)
- C. Elevated sex-hormone binding globulin levels (6%)
- ✓ D. Increased peripheral aromatization of androgens (62%)
- E. Suppression of hypothalamic GnRH secretion (9%)

Omitted
Correct answer
D

62%
Answered correctly

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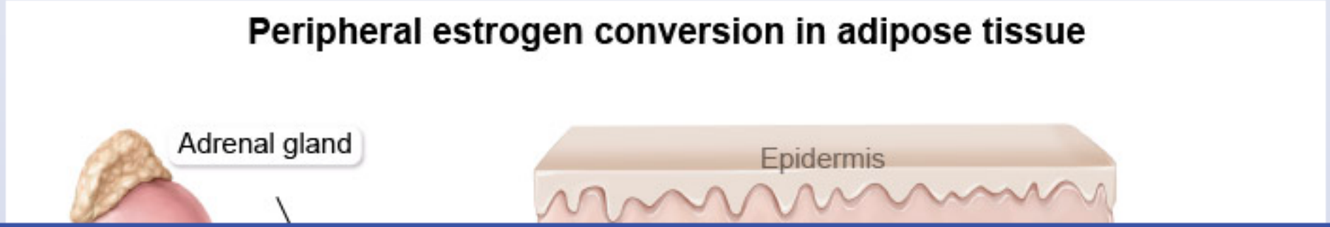
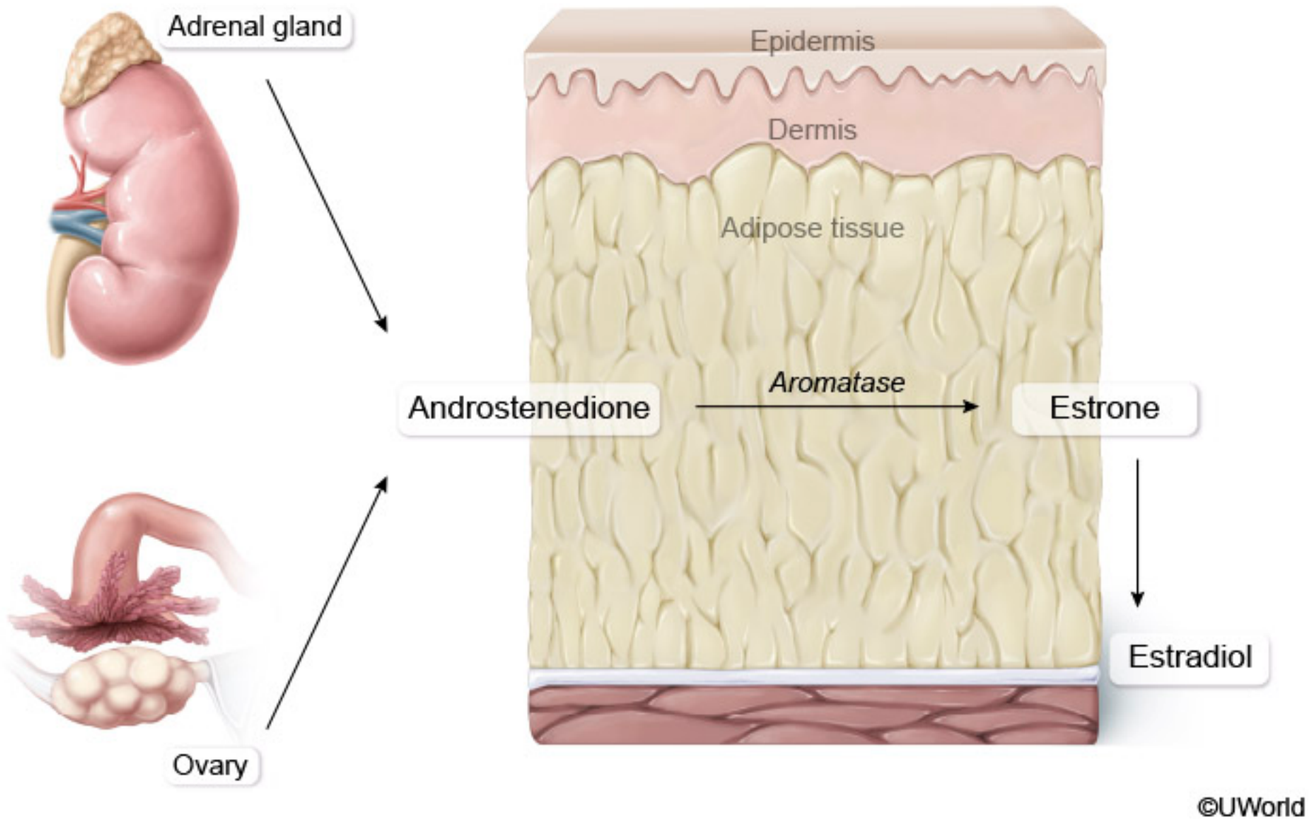
03/30/2020
Last Updated

Explanation



Peripheral estrogen conversion in adipose tissue



This obese patient with **postmenopausal bleeding** most likely has **endometrial hyperplasia or cancer**. The most common risk factor for endometrial hyperplasia/cancer is chronic unopposed estrogen exposure, which is associated with **obesity**, early menarche, late menopause, and chronic anovulation.

Postmenopausal women have decreased ovarian function (ie, low estrogen and progesterone production), resulting in cessation of endometrial proliferation and subsequent amenorrhea. However, small amounts of androgens continue to be produced in the ovaries and adrenal glands after

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Postmenopausal women have decreased ovarian function (ie, low estrogen and progesterone production), resulting in cessation of endometrial proliferation and subsequent amenorrhea. However, small amounts of androgens continue to be produced in the ovaries and adrenal glands after menopause. In obese women, these androgens (eg, androstenedione) are readily converted to estrogens (eg, estrone) by the **aromatase** enzyme found **in adipose tissue**.

The increased peripheral production of estrogens in adipose tissue and the decrease in sex-hormone binding globulin levels (that normally occurs with menopause) lead to elevated free estrogen levels **(Choice C)**. However, ovarian progesterone production remains low; therefore, the **unopposed estrogen** causes **unregulated endometrial proliferation** and subsequent endometrial hyperplasia or cancer, which often presents as postmenopausal or abnormal uterine bleeding.

(Choice A) Hyperprolactinemia due to autonomous pituitary secretion of prolactin (ie, pituitary adenoma) causes negative feedback to the hypothalamus. This results in decreased hypothalamic GnRH secretion, decreased pituitary FSH and LH secretion, and decreased estrogen and progesterone levels. Therefore, premenopausal women often have signs of hyperprolactinemia (eg, galactorrhea) and hypoestrogenism (eg, amenorrhea). In postmenopausal women, the most common symptom is tumor mass effect (eg, headache, bitemporal hemianopsia).

(Choice B) Endometriosis, the ectopic implantation of endometrial glands and stroma, typically causes painful menses (ie, dysmenorrhea) due to inflamed tissue on the peritoneum. Endometriosis is uncommon after menopause because it requires high premenopausal estrogen levels that do not occur even in obese women.

(Choice E) Suppression of hypothalamic GnRH secretion (ie, hypothalamic hypogonadism) most commonly occurs in women with severe caloric restriction (eg, anorexia), excessive energy expenditure (eg, female athlete triad), or stress. The decreased GnRH secretion results in decreased pituitary FSH and LH secretion and subsequent decreased ovarian estrogen and progesterone production. Therefore, patients typically have amenorrhea rather than postmenopausal bleeding.

Educational objective:
Endometrial hyperplasia and cancer often present with postmenopausal bleeding. A common risk factor for endometrial cancer is obesity due to the peripheral aromatization of androgens to estrogens in adipose tissue, which leads to chronic unopposed estrogen exposure and uncontrolled endometrial tissue proliferation.

with menopause) lead to elevated free estrogen levels **(Choice C)**. However, ovarian progesterone production remains low; therefore, the **unopposed estrogen** causes **unregulated endometrial proliferation** and subsequent endometrial hyperplasia or cancer, which often presents as postmenopausal or abnormal uterine bleeding.

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Endometrial hyperplasia and cancer often present with postmenopausal bleeding. A common risk factor for endometrial cancer is obesity due to the peripheral aromatization of androgens to estrogens in adipose tissue, which leads to chronic unopposed estrogen exposure and uncontrolled endometrial tissue proliferation.

References

- Addressing the role of obesity in endometrial cancer risk, prevention, and treatment.

Pathophysiology	Female Reproductive System & Breast	Endometrial cancer
Subject	System	Topic

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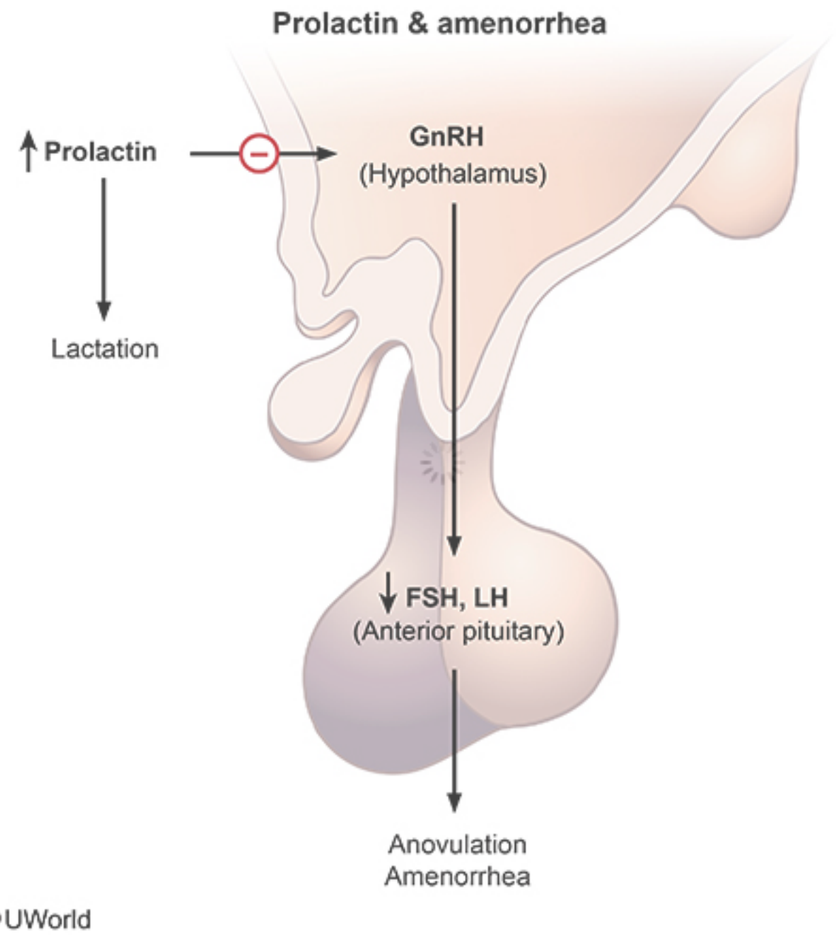

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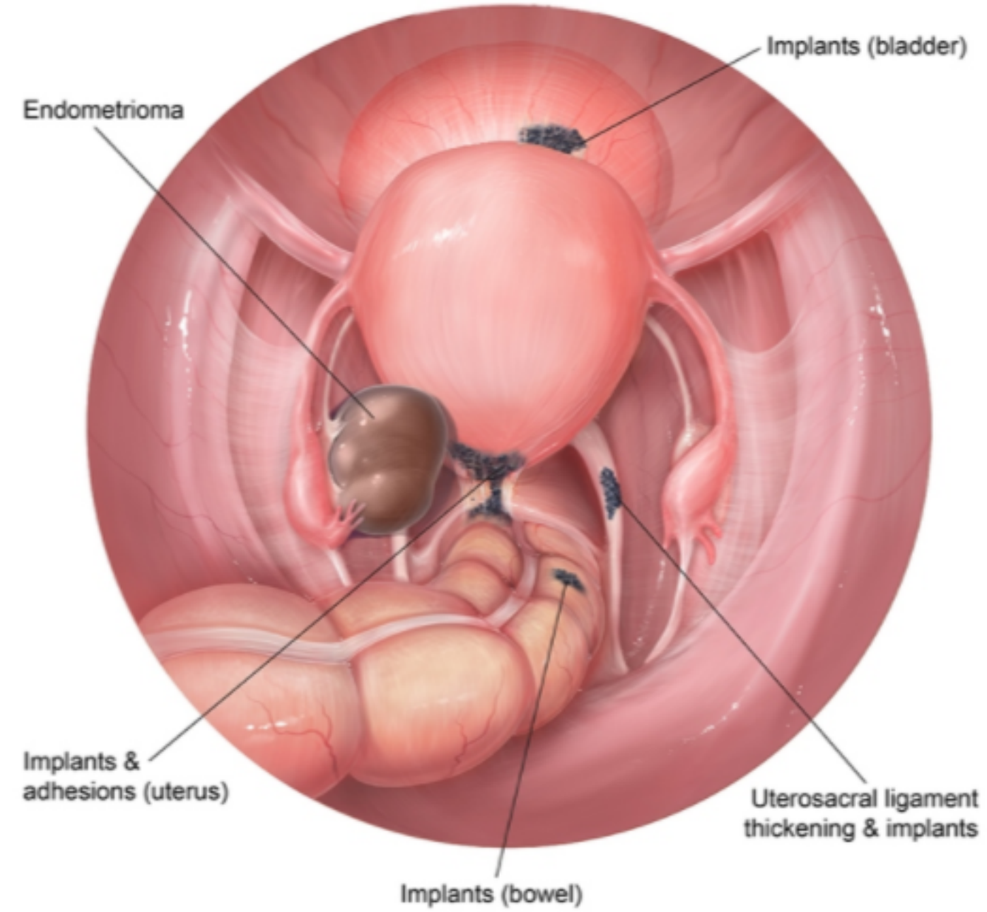
Pelvic endometriosis



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A 35-year-old nulliparous, mildly obese woman is diagnosed with cervical intraepithelial neoplasia III. She has been sexually active for 15 years and has had 4 lifetime partners. She has been monogamous with her current partner for several months and takes oral contraceptives consistently. The patient does not use condoms and douches regularly to "stay fresh." Menarche occurred at age 9, and her menses recur every 28 days and last 6 days. She had a plantar wart a few years ago but otherwise has no medical problems. She drinks 1-2 glasses of wine every night but does not use tobacco or illicit drugs. The patient's mother had breast cancer at age 42. Which of the following is the most significant factor that predisposed this patient to cervical abnormalities?

- A. Alcohol use
- B. Early menarche
- C. Family history of breast cancer
- D. History of plantar wart
- E. Lack of barrier contraception
- F. Nulliparity
- G. Obesity
- H. Practice of douching

Submit

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- A. Alcohol use (0%)
- B. Early menarche (7%)
- C. Family history of breast cancer (5%)
- D. History of plantar wart (8%)
- ✓ E. Lack of barrier contraception (70%)
- F. Nulliparity (3%)
- G. Obesity (0%)
- H. Practice of douching (3%)

Omitted
Correct answer
E

70%
Answered correctly

02 secs
Time Spent

01/15/2020
Last Updated

Explanation

Explanation

HPV strains	Presentation
1-4	Skin warts (verruca vulgaris)
6, 11	Genital warts (condylomata acuminata)
16, 18	Cervical, vaginal, vulvar & anal neoplasia

HPV= human papillomavirus.

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Squamous cell carcinoma (SCC), the most common type of cervical cancer, arises from the squamocolumnar junction of the endocervix. **Cervical intraepithelial neoplasia (CIN)** is **carcinoma in situ** and precedes SCC. CIN represents a wide spectrum of dysplastic changes of the cervical epithelium that occur under the influence of **human papillomavirus (HPV) infection**. CIN is usually transient in young healthy women. However, patients with persistent HPV infection or untreated high-grade CIN are at risk for invasive cervical cancer.

HPV strains 6 and 11 typically cause condylomata acuminata (genital warts) and have low malignancy potential. However, DNA from **high-risk strains (ie, 16, 18, and 31)** is integrated into the human cell genome, leading to overexpression of **viral oncogenes E6 and E7**. E6 binds protein p53 and increases its degradation, whereas E7 binds to the retinoblastoma (*RB1*) gene and displaces transcription factors normally bound by pRB, the tumor suppressor protein product of *RB*.

Risk factors for developing cervical cancer are related to the risk of acquiring HPV infection. Although HPV can be transmitted by skin-to-skin contact, oncogenic strains are spread primarily by sexual contact. Therefore, this patient's most significant risk factors are a history of multiple sexual partners and the **lack of barrier contraceptive** (eg, condom) use.

(Choice A) Alcohol consumption increases the risk of liver and breast cancers, not cervical cancer.

(Choices B, F, and G) Nulliparity, early menarche, and obesity increase the risk of endometrial cancer. These factors are associated with

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(Choice C) Family history of breast cancer is a risk factor for developing breast malignancy. Breast cancer is not associated with cervical cancer, as the latter is usually due to a persistent, oncogenic HPV infection.

(Choice D) A plantar wart is usually caused by HPV strains 1-4; however, these strains are not typically carcinogenic and are not associated with cervical dysplasia and invasive cervical cancer.

(Choice H) Douching is not a risk factor for HPV infection or cervical dysplasia/cancer. However, it is a risk factor for bacterial vaginosis. Douching disturbs the vaginal ecosystem, resulting in overgrowth of *Gardnerella vaginalis*.

Educational objective:
Consistent use of barrier contraceptives is extremely important for preventing sexually transmitted infections, including human papillomavirus (HPV). Patients infected with carcinogenic strains of HPV (ie, 16, 18, and 31) are at risk of squamous cell carcinoma of the cervix.

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(Choice A) Alcohol consumption increases the risk of liver and breast cancers, not cervical cancer.

(Choices B, F, and G) Nulliparity, early menarche, and obesity increase the risk of endometrial cancer. These factors are associated with increased estrogen stimulation of the endometrium.

(Choice C) Family history of breast cancer is a risk factor for developing breast malignancy. Breast cancer is not associated with cervical cancer, as the latter is usually due to a persistent, oncogenic HPV infection.

(Choice D) A plantar wart is usually caused by HPV strains 1-4; however, these strains are not typically carcinogenic and are not associated with cervical dysplasia and invasive cervical cancer.

(Choice H) Douching is not a risk factor for HPV infection or cervical dysplasia/cancer. However, it is a risk factor for bacterial vaginosis. Douching disturbs the vaginal ecosystem, resulting in overgrowth of *Gardnerella vaginalis*.

Educational objective:
Consistent use of barrier contraceptives is extremely important for preventing sexually transmitted infections, including human papillomavirus (HPV). Patients infected with carcinogenic strains of HPV (ie, 16, 18, and 31) are at risk of squamous cell carcinoma of the cervix.

References

- HPV infection and cervical neoplasia: associated risk factors.
- ACOG Practice Bulletin No.131: Screening for cervical cancer.

Pathophysiology	Female Reproductive System & Breast	Cervical cancer
Subject	System	Topic

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A 37-year-old woman, gravida 3 para 1, at 28 weeks gestation comes to the office due to loss of urine with cough. She reports fetal movement and has had an uneventful pregnancy. Several years ago she had a spontaneous vaginal delivery of a 3.5-kg infant. The patient has had no medical problems or surgeries. Her prepregnancy BMI is 32 kg/m^2. She has gained approximately 15.88 kg (35 lb) during this pregnancy. Urine culture is negative. Which of the following is the most likely mechanism for this patient's urinary incontinence?

A. Decreased systemic blood volume
B. Detrusor muscle hyperactivity
C. Increased intraabdominal pressure
D. Sciatic nerve root compression
E. Ureteral compression
F. Urinary tract infection

Submit

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- A. Decreased systemic blood volume (0%)
- B. Detrusor muscle hyperactivity (4%)
- ✓ C. Increased intraabdominal pressure (86%)
- D. Sciatic nerve root compression (1%)
- E. Ureteral compression (6%)
- F. Urinary tract infection (0%)

Omitted
Correct answer
C

86%
Answered correctly

01 sec
Time Spent

03/10/2020
Last Updated

Explanation

Differential diagnosis of urinary incontinence		
	Etiology	**Symptoms**
Stress	↓ Urethral sphincter tone	Leakage with coughing, lifting, sneezing

Explanation

Differential diagnosis of urinary incontinence		
	Etiology	**Symptoms**
Stress	↓ Urethral sphincter tone Urethral hypermobility	Leakage with coughing, lifting, sneezing
Urge	Detrusor hyperactivity	Sudden, overwhelming urge to urinate
Overflow	Impaired detrusor contractility Bladder outlet obstruction	Incomplete emptying & persistent involuntary dribbling

Stress urinary incontinence is a common and bothersome symptom during pregnancy. Physiologic changes in pregnancy include an increase in plasma volume **(Choice A)** to accommodate potential blood loss during parturition. A rise in glomerular filtration rate occurs with increased renal circulation mediated by the hormone relaxin, which is in turn stimulated by β-hCG. These changes result in a greater volume of urine and lead to increased urinary frequency due to unchanged and eventually diminished bladder capacity from direct compression of the bladder by the fetus. The gravid uterus and maternal weight gain **increase intraabdominal pressure**. In addition, pregnancy hormones decrease urethral tone and relax the pelvic floor muscles (**levator ani, coccygeus**), which function with the urethral valve to maintain continence. Laughing, coughing, and other exertions cause sudden additional increases in intraabdominal pressure and exceed the pressure point that maintains closure of the urethral valve. Forced opening of the valve results in urine leakage. **Kegel exercises** strengthen the pelvic floor muscles and can improve symptoms of stress urinary incontinence.

(Choice B) Urge incontinence is characterized by involuntary detrusor muscle contractions ("overactive bladder") before the bladder is full. Patients typically have frequent loss of large amounts of urine or urgency with small voiding amounts. These symptoms are not associated with exertional activities or cough.

(Choice D) The sciatic nerve can become compressed due to increased joint laxity from circulating relaxin and changes in maternal posture (eg, spinal lordosis). Sciatica commonly presents as low back pain radiating down one side of the hip to the leg, without urinary incontinence.

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(Choice D) The sciatic nerve can become compressed due to increased joint laxity from circulating relaxin and changes in maternal posture (eg, spinal lordosis). Sciatica commonly presents as low back pain radiating down one side of the hip to the leg, without urinary incontinence.

(Choices E and F) The gravid uterus causes ureteral compression that may result in physiologic hydronephrosis (eg, dilation of the ureter). Although ureteral dilation does not cause incontinence, the resulting urinary stasis becomes a breeding ground for bacteria and predisposes pregnant women to urinary tract infections. Negative urine culture denotes a lack of bacteriuria and effectively rules out infection.

Educational objective:
A common symptom during pregnancy is stress urinary incontinence, which occurs due to increased intraabdominal pressure from the gravid uterus that exceeds the pressure point that maintains closure of the urethral valve. Pregnancy hormones decrease urethral tone and relax the pelvic floor muscles (levator ani, coccygeus), which maintain closure of the urethral valve.

References

- Stress urinary incontinence in pregnant women: a review of prevalence, pathophysiology, and treatment.
- The prevalence of urinary incontinence 20 years after childbirth: a national cohort study in singleton primiparae after vaginal or caesarean delivery.

Pathophysiology	Female Reproductive System & Breast	Urinary incontinence
Subject	System	Topic

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A 60-year-old woman, gravida 1, para 1, comes to the office with abdominal distension and decreased appetite. She also has lost 10 pounds (4.5 kg) unintentionally over the past few months. She takes no medications and has received all recommended vaccinations except for the human papilloma vaccine. The patient's mother had *BRCA*-positive ovarian cancer and died at the age of 55. BMI is 30kg/m^2. Imaging studies reveal a right-sided ovarian mass and an accumulation of free peritoneal fluid. Her blood work shows a marked elevation of CA-125. Which of the following most likely would have reduced the risk of this patient's condition?

A. Consistent condom use

B. Long-term antioxidant supplementation

C. Nulliparity

D. Use of oral contraceptives

E. Vaccination

Submit

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- A. Consistent condom use (3%)
- B. Long-term antioxidant supplementation (10%)
- C. Nulliparity (8%)
- ✓ D. Use of oral contraceptives (70%)
- E. Vaccination (7%)

Omitted
Correct answer
D

70%
Answered correctly

02 secs
Time Spent

06/28/2020
Last Updated

Explanation

Epithelial ovarian cancer	
	• Family history • Infertility • Nulliparity

Explanation

Epithelial ovarian cancer	
Risk factors	• Family history • Infertility • Nulliparity • Polycystic ovarian syndrome • Endometriosis • *BRCA1* or *BRCA2* mutations • Lynch syndrome • Postmenopausal hormone therapy
Protective factors	• Combined oral contraceptives • Multiparity • Breastfeeding • Salpingo-oophorectomy

This patient's presentation is most likely due to **epithelial ovarian cancer (EOC)**. Common manifestations include abdominal distension, ascites, pleural effusion, bowel obstruction, decreased appetite, weight loss, and an ovarian mass. Patients with EOC often present with advanced disease and increased mortality risk due to the lack of effective screening methods. **Cancer antigen 125 (CA-125)** is a protein produced by ovarian epithelia and is usually markedly elevated in cancerous ovarian cells compared to normal cells. However, CA-125 is neither sensitive nor specific for early EOC as it can be found in normal tissue and other cancers.

Women with ***BRCA* mutations** are at significantly increased risk for ovarian cancer. Additional **risk factors** include repeated ovulation, such as nulliparity **(Choice C)** or ovarian dysfunction (eg, infertility). These conditions inflict minor trauma to the ovarian surface, therefore rendering the epithelia susceptible to transformation.

Protective factors include **oral contraceptives**, multiparity, and breastfeeding. The common mechanism of these protective factors is less repair at the ovarian surface due to reduced lifetime ovulation frequency.

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Protective factors include **oral contraceptives**, multiparity, and breastfeeding. The common mechanism of these protective factors is less repair at the ovarian surface due to reduced lifetime ovulation frequency.

(Choices A and E) Consistent condom use and the human papilloma virus (HPV) vaccine can reduce transmission of high-risk HPV, which in turn can reduce the risk of cervical, vaginal, and vulvar cancer in women. HPV infection is not linked to ovarian cancer.

(Choice B) Antioxidants neutralize reactive oxygen species and free radicals, thereby decreasing their damage to cells. However, long-term antioxidant supplementation (eg, vitamin C) has not been proven to decrease the risk of any cancer, including ovarian cancer.

Educational objective:
The pathogenesis of epithelial ovarian cancer is linked to the frequency of trauma and repair at the ovarian surface. Oral contraceptives, multiparity, and breastfeeding are protective by decreasing the frequency of ovulation. Risk factors include *BRCA* mutation, nulliparity, and infertility.

References

- ACOG Practice Bulletin No. 89. Elective and risk reducing salpingo-oophorectomy
- Hormone prevention strategies for breast, endometrial and ovarian cancers.
- Ovarian cancer molecular pathology.

Pathophysiology	Female Reproductive System & Breast	Ovarian cancer
Subject	System	Topic

A 17-year-old boy comes to the office for evaluation of gynecomastia. Examination shows sparse facial and pubic hair. Laboratory studies show:

Serum testosterone	high
Serum LH	high
Serum FSH	normal

Semen analysis reveals severe oligospermia. Which of the following mechanisms is the most likely cause of this patient's condition?

A. Androgen receptor dysfunction
B. Damage to seminiferous tubules
C. Ejaculatory duct obstruction
D. Exogenous androgen use
E. Impaired Leydig cell function

Submit

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Serum testosterone	high
Serum LH	high
Serum FSH	normal

Semen analysis reveals severe oligospermia. Which of the following mechanisms is the most likely cause of this patient's condition?

- ✓ A. Androgen receptor dysfunction (75%)
- B. Damage to seminiferous tubules (6%)
- C. Ejaculatory duct obstruction (0%)
- D. Exogenous androgen use (11%)
- E. Impaired Leydig cell function (5%)

Omitted
Correct answer
A

75%
Answered correctly

02 secs
Time Spent

05/08/2020
Last Updated

Explanation

Hormonal changes in oligospermia	
Ejaculatory duct obstruction	• Normal FSH, LH, testosterone

Hormonal changes in oligospermia	
Ejaculatory duct obstruction	• Normal FSH, LH, testosterone
Primary hypogonadism	• Low testosterone • Elevated FSH, LH
Secondary (hypogonadotropic) hypogonadism	• Low testosterone • Low/normal FSH, LH
Partial androgen resistance	• Elevated LH, testosterone • Normal FSH

This patient has an **elevated testosterone** level, but his gynecomastia and sparse facial and pubic hair suggests lack of the expected physiologic response. **Androgen insensitivity syndrome (AIS)** is caused by **loss-of-function** mutations of the **androgen receptor** (AR) gene on the X chromosome. Complete AIS is characterized by female body habitus and external genitalia (but with absence of internal Mullerian derivatives) and cryptorchid testes. In contrast, **partial AIS** has a variable phenotype; typical findings include:

- **Undervirilization** of the external genitalia, ranging from phenotypically female to phenotypically male (often with microphallus and hypospadias)
- Decreased facial, axillary, and pubic hair (which is driven by androgens in both males and females)
- **Oligospermia**
- **Gynecomastia**

Dysfunction of the AR in the hypothalamus and pituitary leads to loss of feedback inhibition of gonadotropin-releasing hormone (GnRH), FSH, and LH. This results in the following hormonal findings:

- GnRH induces **increased LH secretion**, which leads to **increased testosterone production** in the testes.
- FSH secretion is increased by GnRH but suppressed by inhibin from the seminiferous tubules and is often normal.

Exhibit Display

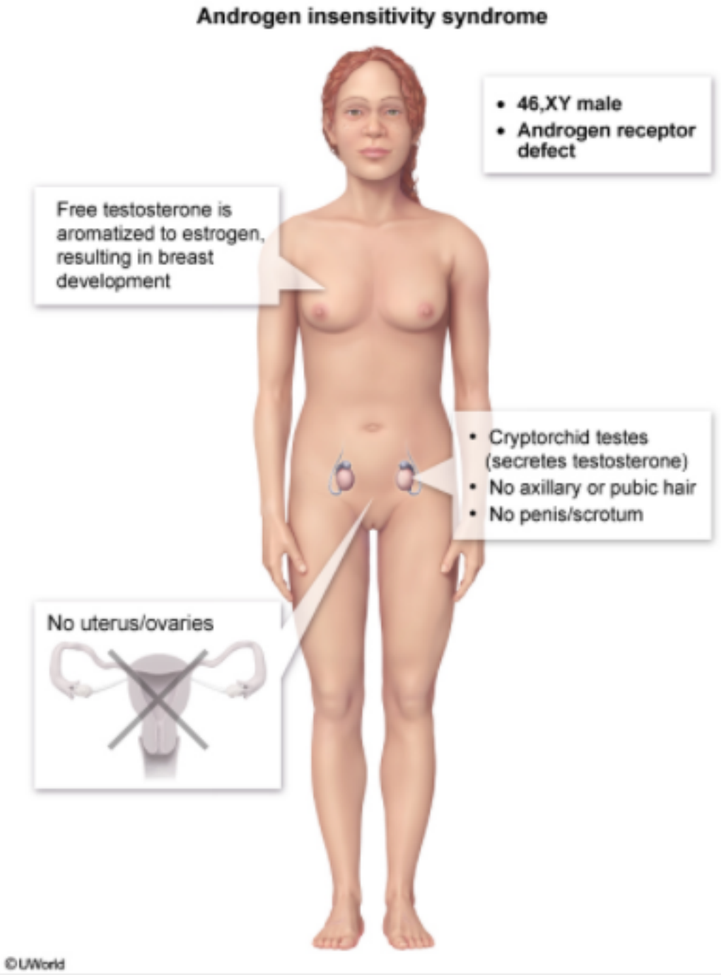

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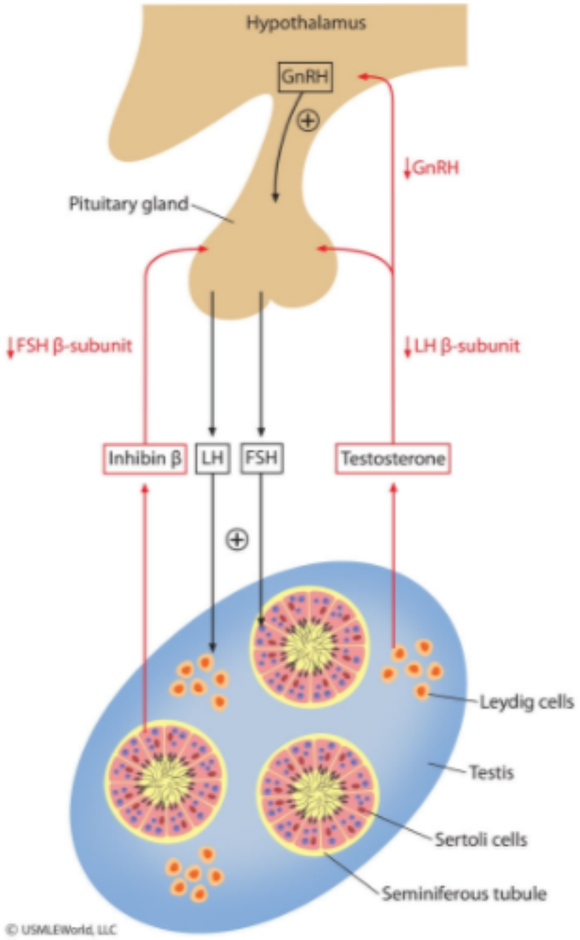
Exhibit Display

Gonadotropin regulation



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- **Oligospermia**
- **Gynecomastia**

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- GnRH induces **increased LH secretion**, which leads to **increased testosterone production** in the testes.
- FSH secretion is increased by GnRH but suppressed by inhibin from the seminiferous tubules and is often normal.
- Estrogen, which is derived by aromatization of testosterone, may be normal or elevated.

(Choices B and E) Testicular disorders can affect the Leydig cells, seminiferous tubules, or both. The Leydig cells are the primary site of testosterone production; reduced Leydig cell function can cause gynecomastia and elevated LH but would be associated with low (not high) testosterone. Injury to the seminiferous tubules leads to loss of inhibin feedback of FSH secretion and an elevated FSH.

(Choice C) Ejaculatory duct obstruction can be caused by congenital defects or infection (eg, *Chlamydia trachomatis*). Sperm counts are low but testicular endocrine function (ie, testosterone level) is typically normal.

(Choice D) Abuse of exogenous androgens can reduce spermatogenesis (due to reduced local testicular testosterone levels) and cause gynecomastia (due to aromatization of excess androgens to estrogens). However, this would be associated with suppression of LH levels.

Educational objective:
Androgen receptor dysfunction in patients with partial androgen insensitivity syndrome leads to decreased facial, axillary, and pubic hair; oligospermia; gynecomastia; and undervirilization of external genitalia (eg, microphallus). Loss of feedback inhibition of gonadotropin-releasing hormone results in elevated LH and testosterone levels.

Pathophysiology	Male Reproductive System	Infertility
Subject	System	Topic

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